WEST Search History

DATE: Tuesday, August 20, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=AND		
L24	l14 or l17 or l20 or L23	3	L24
L23	l11 and L22	3	L23
L22	jeffrey.in. and L21	49	L22
L21	seilhamer.in.	49	L21
L20	l11 and L19	3	L20
L19	olga.in. and L18	221	L19
L18	bandman.in.	222	L18
L17	l11 and L16	3	L17
L16	janice.in. and L15	82	L16
L15	au-young.in.	82	L15
L14	l11 and L13	3	L14
L13	roger.in. and L12	40	L13
L12	coleman.in.	1469	L12
L11	l9 and L10	35	L11
L10	isolate or isolated	349792	L10
L9	l3 and L8	35	L9
L8	l5 or l6 or L7	49620	L8
L7	nucleotide	37380	L7
L6	nucleic adj acid	41096	L6
L5	polynucleotide	15220	L5
L4	l3 and polynucleotide	9	L4
L3	l1 or L2	43	L3
L2	human near thrombin near receptor	43	L2
L1	human adj thrombin adj receptor	43	L1

END OF SEARCH HISTORY

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:48:09 ON 20 AUG 2002

=> file biosis medline caplus

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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FILE 'CAPLUS' ENTERED AT 18:48:20 ON 20 AUG 2002
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=> human thrombin receptor

L1          267 HUMAN THROMBIN RECEPTOR

=> human(s)thrombin(s)receptor

L2         3726 HUMAN(S) THROMBIN(S) RECEPTOR

=> ?nucle?

   2 FILES SEARCHED...
L3      3700239 ?NUCLE?

=> l2 and l3

L4          507 L2 AND L3

=> isolat?

L5      2534191 ISOLAT?

=> l4 and l5

L6           60 L4 AND L5

=> l6 and 1970-1995/py

   2 FILES SEARCHED...
L7           38 L6 AND 1970-1995/PY

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8           31 DUP REM L7 (7 DUPLICATES REMOVED)

=> l1 and l3

L9           56 L1 AND L3

=> l9 and l5
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L10           9 L9 AND L5

=> l10 and 1970-1995/py

   2 FILES SEARCHED...
L11           5 L10 AND 1970-1995/PY

=> dup rem

ENTER L# LIST OR (END):l11

PROCESSING COMPLETED FOR L11
L12           5 DUP REM L11 (0 DUPLICATES REMOVED)

=> coleman?/au

L13       26502 COLEMAN?/AU

=> roger?/au

L14       51775 ROGER?/AU

=> l13 and l14

L15          59 L13 AND L14

=> l8 and l15

L16           0 L8 AND L15

=> au-young?/au

L17         259 AU-YOUNG?/AU

=> janice?/au

L18         661 JANICE?/AU

=> l17 and l18

L19           0 L17 AND L18

=> bandman?/au

L20        1009 BANDMAN?/AU

=> olga?/au

L21         847 OLGA?/AU

=> l20 and l21

L22           0 L20 AND L21

=> seilhamer?/au

L23         248 SEILHAMER?/AU

=> jeffrey?/au
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L24 6877 JEFFREY?/AU

=> l23 and l24

L25 0 L23 AND L24

=> d l12 ti abs so 1-5

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
TI **Human thrombin receptors** are insensitive to thrombin-like snake venom enzymes
AB Thrombin-like snake venoms enzymes, flavoxobin, and okinaxobin I **isolated** from Trimeresurus flavoviridis and Trimeresurus okinavensis, resp., were examd. in SHEP cells and evaluated whether or not they can activated **human thrombin receptors**. Flavoxobin was almost completely inactive in both assays for phosphoinositide turnover and DNA synthesis. In contrast, okinaxobin I stimulated phosphoinositide turnover in a dose dependent manner, but considerably weakly. The EC50 value was about 100 nM, which was 4,000 times larger than that of .alpha.-thrombin. This stimulation was not inhibited by hirudin, and effective inhibitor of .alpha.-thrombin. Okinaxobin I also induced a very weak stimulation of DNA synthesis. These results suggest that thrombin-like snake venom enzymes interact with **human thrombin receptors** in inefficient ways. Weak interactions of the enzymes with thrombin receptor and inhibitor were ascribed to the incomplete formation of a lysine-cation cluster necessary for electrostatic mol. recognition.
SO Biochem. Mol. Biol. Int. (**1995**), 35(2), 415-21
CODEN: BMBIES; ISSN: 1039-9712

L12 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Chromosomal assignment of the **human thrombin receptor** gene: Localization to region q13 of chromosome 5.
AB A functional thrombin receptor (TR) structurally related to other members of the seven-transmembrane receptor family has been **isolated** from diverse cellular types intimately involved in the regulation of the thrombotic response. This receptor recapitulates many of the previously identified sequelae of thrombin-mediated cell activation phenomenon, and requires proteolytic cleavage for downstream effector response coupling events. Using two complementary approaches, we have now completed the chromosomal assignment of the **human thrombin receptor** gene. Discordancy analysis of polymerase chain reaction products from a human-rodent hybrid cell mapping panel assigned the sequence to human chromosome 5 with no observed discordancies. Cytogenetic localization using fluorescence in situ hybridization on human metaphase chromosomes specifically localized the human TR gene to region q13 of chromosome 5, confirming its presence as a single-locus gene in the human genome. The chromosomal localization of the human TR gene is at or contiguous with the proximal breakpoint site identified in the majority of patients with the 5q - syndrome (dysmegakaryocytopoiesis and refractory anemia).
SO Blood, (1993) Vol. 82, No. 5, pp. 1532-1537.
ISSN: 0006-4971.

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
TI The thrombin receptor extracellular domain contains sites crucial for peptide ligand-induced activation
AB A thrombin receptor (TR) demonstrating a unique activation mechanism has recently been **isolated** from a megakaryocytic (Dami) cell line. To further study determinants of peptide ligand-mediated activation phenomenon, the authors have **isolated**, cloned, and stably expressed the identical receptor from a human umbilical vein endothelial cell (HUVEC) library. CHO cells expressing a functional TR (CHO-TR), platelets, and HUVECs were then used to specifically characterize .alpha.-thrombin- and peptide ligand-induced activation responses using 2 different antibodies: anti-TR34-52 directed against a 20-amino-acid peptide spanning the thrombin cleavage site, and anti-TR1-160 generated against the N-terminal 160 amino acids of the TR expressed as a chimeric protein in Escherichia coli. Activation-dependent responses to both .alpha.-thrombin (10 nM) and peptide ligand (20 .mu.M) were studied using fura 2-loaded cells and microspectrofluorimetry. Whereas preincubation of CHO-TR with anti-TR34-52 abolished only .alpha.-thrombin-induced intracellular Ca2+ concn. ([Ca2+]i) transients, preincubation with anti-TR1-160 abrogated both .alpha.-thrombin- and peptide ligand-induced responses. This latter inhibitory effect was dose dependent and similar for both agonists, with an EC50 of .apprx.90 .mu.g/mL. Anti-TR1-160 similarly abolished peptide ligand-induced [Ca2+]i transients in platelets and HUVECs, whereas qual. different responses characterized by delayed but sustained elevations in [Ca2+]i transients were evident using .alpha.-thrombin. Platelet aggregation to low concns. of both ligands was nearly abolished by anti-TR1-160, although some shape change remained; anti-TR34-52 only inhibited .alpha.-thrombin-induced aggregation. These data established that a crit. recognition sequence for peptide ligand-mediated receptor activation is contained on the N-terminal portion of the receptor, upstream from the 1st transmembrane domain. Furthermore, .alpha.-thrombin-induced activation of HUVECs and platelets may be partially mediated by an alternative mechanism(s) or receptor(s).
SO J. Clin. Invest. (**1993**), 91(4), 1405-13
CODEN: JCINAO; ISSN: 0021-9738

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
TI Molecular cloning of the rat vascular smooth muscle thrombin receptor. Evidence for in vitro regulation by basic fibroblast growth factor
AB To study thrombin's receptor-mediated effects on vascular cells, a cDNA encoding a rat smooth muscle cell thrombin receptor was **isolated** and characterized. A rat aortic smooth muscle (RASM) cell cDNA library was screened with a 500-base pair (bp) sequence from the **human thrombin receptor**, obtained by polymerase chain reaction (PCR) amplification of cDNA synthesized from human erythropoietic leukemia (HEL) cell mRNA with PCR primers based on the published **human thrombin receptor** sequence. Clone pRTHR17 contains a 3418-bp insert that includes 50 bp of the 5'-untranslated region and the entire coding and 3'-untranslated regions of the RASM cell thrombin receptor. The sequence of pRTHR17 is 85% similar, at the **nucleotide** level, and 78% similar, at the deduced amino acid level, to the **human thrombin receptor**.

Although the putative thrombin cleavage and binding sites are present, there are significant differences between the rat and human receptors in their amino-terminal sequences. Detectable signals (consisting of a single band of 3.45 kb) are present by Northern anal. of mRNA from RASM cells, and rat lung, kidney, and testes, but not in aorta or other tissues probed. The results of Southern anal. of rat genomic DNA are consistent with the existence of a single copy of the gene encoding this receptor. The steady state thrombin receptor mRNA level is low in cultured growth-arrested RASM cells and not detectable in rat aorta. To det. whether regulation of the RASM cell thrombin receptor occurs under growth-stimulating conditions, growth-arrested RASM cells were treated with basic fibroblast growth factor. There was a significant increase in thrombin receptor mRNA following the addn. of bFGF. These data demonstrate that: 1) mRNA for a thrombin receptor similar to that reported from human megakaryocyte and hamster fibroblast cell lines is present in proliferating primary cultured rat smooth muscle cells, 2) the most significant sequence differences are present in the amino-terminal tail of the thrombin receptor, and 3) the mRNA level for this receptor is regulated under growth-stimulating conditions in vitro.
SO J. Biol. Chem. (**1992**), 267(24), 16975-9
CODEN: JBCHA3; ISSN: 0021-9258

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
TI Molecular cloning of a functional thrombin receptor reveals a novel proteolytic mechanism of receptor activation
AB A cDNA encoding a functional **human thrombin receptor** was **isolated** by direct expression cloning in Xenopus oocytes. The mRNA encoding this receptor was detected in human platelets and vascular endothelial cells. The deduced amino acid sequence revealed a new member of the seven transmembrane domain receptor family with a large amino-terminal extracellular extension contg. a remarkable feature. A putative thrombin cleavage site (LDPR/S) resembling the activation cleavage site in the zymogen protein C (LDPR/I) was noted 41 amino acids carboxyl to the receptor's start methionine. A peptide mimicking the new amino terminus created by cleavage at R41 was a potent agonist for both thrombin receptor activation and platelet activation. Uncleavable mutant thrombin receptors failed to respond to thrombin but were responsive to the new amino-terminal peptide. These data reveal a novel signaling mechanism in which thrombin cleaves its receptor's amino-terminal extension to create a new receptor amino terminus that functions as a tethered ligand and activates the receptor.
SO Cell (Cambridge, Mass.) (**1991**), 64(6), 1057-68
CODEN: CELLB5; ISSN: 0092-8674

=> d his

(FILE 'HOME' ENTERED AT 18:48:09 ON 20 AUG 2002)

FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 18:48:20 ON 20 AUG 2002
L1 267 HUMAN THROMBIN RECEPTOR
L2 3726 HUMAN(S)THROMBIN(S)RECEPTOR
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L22            0 L20 AND L21
L23          248 SEILHAMER?/AU
L24         6877 JEFFREY?/AU
L25            0 L23 AND L24
L26           38 DHIS

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